Oral prednisolone for 4 days does not increase exercise tolerance in men with COPD

Karlsson, SL; Backer, V; Godtfredsen, Nina Skavlan

Published in:
Chronic Respiratory Disease

DOI:
10.1177/1479972317721929

Publication date:
2018

Document version
Publisher's PDF, also known as Version of record

Research letter

Chronic Respiratory Disease

Chronic Respiratory Disease
2018, Vol. 15(2) 220–222

DOI: 10.1177/1479972317721929
journals.sagepub.com/home/crd
SAGE

Oral prednisolone for 4 days does not increase exercise tolerance in men with COPD

SL Karlsson[1], V Backer[2] and Nina Skavlan Godtfredsen[1]

Abstract

One of the primary objectives in management of chronic obstructive pulmonary disease (COPD) is preventing decrease in lung function and reducing the annual number of acute exacerbations of COPD (AECOPD). An oral course of systemic corticosteroids is a commonly used treatment in AECOPD. We hypothesize that this treatment also increases exercise performance and decreases muscle fatigue. In a randomized double-blinded, parallel, placebo-controlled trial, we investigated 14 men (8 on prednisolone 37.5 mg vs. 6 on placebo) with severe and very severe COPD. For 5 consecutive days, the patients performed a submaximal endurance test measuring time to exhaustion (TTE, primary endpoint), spirometry, maximal inspiratory and expiratory pressure and maximal isometric contraction of the quadriceps femoris muscle (maximum voluntary contraction (MVC)). At visits 2, 3 and 4, a fatigue protocol was carried out after 40 minutes of cycling at 40% of maximal effort. No differences between groups were found for TTE, lung function or maximal inspiratory or expiratory pressure, however, patients on prednisolone showed significant increased MVC: median 5.15 [3.35; 9.15] against placebo: −2 [−5.57; 3.95] ($p = 0.03$). This finding indicates an impact of corticosteroids on muscle groups being exposed to submaximal endurance.

Keywords

COPD, prednisolone, exercise tolerance, muscle strength

Date received: 15 February 2017; accepted: 12 June 2017

Although oral corticosteroids are not recommended in stable chronic obstructive pulmonary disease (COPD), there is evidence of a subjective feeling of well-being among patients with COPD, a term often referred to as steroid euphoria.[1] This subjective benefit has however not shown to improve the maximal oxygen consumption (VO_{2max}) in COPD patients.[2] One study confirmed the effect of corticosteroids in healthy individuals by administering 60 mg of prednisolone daily for 7 days, showing an increased time to exhaustion (TTE) at 70–75% of VO_{2max}.[3] The mechanisms might be attributed to an impaired sensation of fatigue, reduced muscle inflammation after exercise or to increased availability of metabolic substrates during exercise (glucose and free fatty acids).[4] The aim of this study was to investigate whether 4 days of oral

[1] Department of Respiratory Medicine, Hvidovre University Hospital, Hvidovre, Denmark
[2] Respiratory Research Unit, Department of Respiratory Medicine, Bispebjerg University Hospital, Copenhagen, Denmark

Corresponding author:
Nina Skavlan Godtfredsen, Department of Respiratory Medicine, Hvidovre University Hospital, Kettegård Allé 30, 2650 Hvidovre, Denmark.
Email: Nina.Skavlan.Godtfredsen@regionh.dk

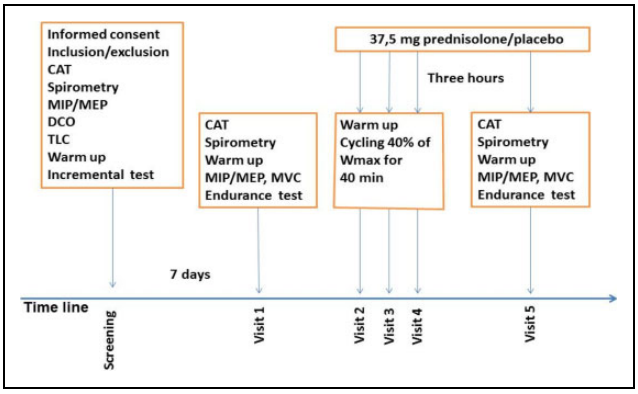

Figure 1. Flowchart of the study.

corticosteroids could preserve or increase exercise tolerance and muscle strength in stable COPD patients after performing a fatigue protocol.

The study was a randomized, double-blinded, parallel design with eight participants receiving 37.5 mg of prednisolone and six participants receiving placebo. Approval was obtained from local and national ethics committees (nos H-3-2012-142/ EudraCT 2012-004503-13). The study consisted of six visits: one baseline visit 5–7 days before five consecutive daily visits. At the baseline visit, eligibility was determined, and spirometry, body plethysmography, COPD Assessment Test (CAT), diffusion capacity (D_LCO) and an incremental exercise test were performed. At visit 1, spirometry, CAT and maximal inspiratory/expiratory pressure (MIP/MEP) were assessed followed by a 5-minute warm up at 10% W_{max} and 20 minutes at 40% W_{max}. A maximum voluntary contraction (MVC) of the quadriceps muscle on the participant's leading leg was then followed. After 5 minutes' recovery, participants performed a submaximal exercise test (SMET) at 70% W_{max} according to ERS guidelines[5] to measure TTE. At visits 2, 3 and 4, participants performed a 5-minute warm up at 10% W_{max} followed by two constant workload cycling tests at 40% W_{max} of 20 minutes separated by 4 minutes' recovery. On visit 5, participants performed the same protocol as on visit 1. At visits 2, 3, 4 and 5, participants were instructed to take the investigated medicinal product 3 hours before the study visit (Figure 1). For the statistical analysis, students *t*-tests and Mann–Whitney *U* tests were performed using SPSS (IBM, Version 19.0).

Of the 16 screened patients, 14 were randomized and 2 were excluded. Baseline characteristics are presented in Table 1. Nine patients were on LAMA, two on LABA, nine on LABA/ICS, nine on SABA, two on SAMA/SABA, one on ICS monotherapy, one on phosphodiesterase inhibitors and only one was a current smoker. No difference was found in TTE between the prednisolone and the placebo group $p = 0.88$ (Table 2), however, both groups showed improvements in TTE from visit 1 to visit 5 (data not shown). For the secondary outcomes, there were no significant changes either except for MVC, which was significantly higher in the prednisolone group ($p = 0.03$).

Table 1. Baseline characteristics of the included patients.

$N = 14$	Mean	SD
FEV_1, l	1.02	0.46
FEV_1, %	30.55	12.8
FVC, l	2.44	0.79
FVC, %	56.71	15.29
FEV_1/FVC, %	41.49	11.8
RV, l	4.96	1.37
RV, %	201.8	61.7
TLC, l	8.52	1.57
TLC, %	119.4	22.1
RV/TLC, %	57.4	8.3
D_LCO SB	4.43	1.48
D_LCO VA	0.89	0.30
BMI	23.6	4.8
Pack years	44	18.9
CAT score	14	5.2
Age	62.7	6.71
VO_{2max}	15.86	4.43
W_{max}	75.0	27.6

SD: standard deviation; FEV_1: forced expiratory volume in 1 second; FVC: forced vital capacity; RV: residual volume; TLC: total lung capacity; D_LCO/VA: diffusing capacity of the lung for carbon monoxide/alveolar volume; BMI: body mass index; COPD: chronic obstructive pulmonary disease; CAT: COPD Assessment Test; SB: single breath; VO_{2max}: maximal oxygen consumption; W_{max}: maximal work load at the incremental test.

The observed improvement in the SMET in this study is probably due to familiarization with the procedure. Accordingly, the TTE on visit 5 might represent the participants' most accurate exercise tolerance. In previous studies using the SMET, the majority of participants had mild to moderate COPD,[5] whereas the patients in this study had very low lung function and were not accustomed to strenuous exercise. Although not powered, the MVC was significantly lower on visit 5 in the placebo group than in the prednisolone group, indicating an increase in muscle strength following the 3 days' cycling. This finding is in accordance with a previous study.[6]

Table 2. Results of the primary and secondary outcomes after the study.

Delta values	Prednisolone $N = 7$	Placebo = 5	
v5–v1	Median [CI 25–75]	Median [CI 25–75]	*p* Value
FEV_1, l	−0.01 [0.03; −0.01]	0.0 [−0.5; 0.1]	0.07
FEV_1, % predicted	−1.0 [−2.0; 0.0]	0.0 [−1.5; 3.0]	0.18
FVC, l	−0.014 [−0.21; −0.05]	0.15 [−1.0; 0.39]	0.03[a]
FVC, % predicted	−4.0 [−4.0; −1.0]	3.0 [−2.5; 9.5]	0.03[a]
MIP	−6.0 [−20.0; −4.0]	5.0 [3.0; 9.5]	0.054
MEP	4.0 [−11.0; 20.0]	−7.0 [−10.0; −3.0]	0.37
CAT	−2 [−3.0; 1.0]	−1.0 [−2.0; 1.5]	0.22
BORG dyspnea	0 [−1.0; 1.0]	0.0 [−1.5; 1.5]	0.95
BORG leg discomfort	1 [0.0; 1.0]	2.0 [3.0; 9.5]	0.83
TTE	51 [−13; 110]	13 [−18; 208]	0.88
MVC	5.15 [3.35; 9.15]	−2 [−5.57; 3.95]	0.03[a]

CI: confidence interval; FEV_1: forced expiratory volume in 1 second; FVC: forced vital capacity; MIP: maximal inspiratory pressure; MEP: maximal expiratory pressure; COPD: chronic obstructive pulmonary disease; CAT: COPD Assessment Test; TTE: time to exhaustion; MVC: maximal voluntary contraction.
[a]Significant difference between active and placebo group.

Future studies are warranted for evaluation of the effect of short-term systemic corticosteroid in cardiopulmonary measures of strenuous exercise in severe and very severe COPD.

Acknowledgements

The authors would like to thank the August Krogh Institute, University of Copenhagen for use of equipment.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: The study was financially supported from the Danish Lung Foundation, the Becket Foundation and the Respiratory Research Unit at Bispebjerg University Hospital, Copenhagen, Denmark.

References

1. Swinburn CR, Wakefield JM, Newman SP, et al. Evidence of prednisolone induced mood change ('steroid euphoria') in patients with chronic obstructive airways disease. *Br J Clin Pharmacol* 1988; 26: 709–713.
2. Strain DS, Kinasewitz GT, Franco DP, et al. Effect of steroid therapy on exercise performance in patients with irreversible chronic obstructive pulmonary disease. *Chest* 1985; 88: 718–721.
3. Collomp K, Arlettaz A, Portier H, et al. Short-term glucocorticoid intake combined with intense training on performance and hormonal responses. *Br J Sports Med* 2008; 42: 983–988.
4. Soetens E, De Meirleir K and Hueting JE. No influence of ACTH on maximal performance. *Psychopharmacology* 1995; 118: 260–266.
5. Puente-Maestu L, Palange P, Casaburi R, et al. Use of exercise testing in the evaluation of interventional efficacy: an official ERS statement. *Eur Respir J* 2016; 47: 429–460.
6. Hopkinson NS, Man WD, Dayer MJ, et al. Acute effect of oral steroids on muscle function in chronic obstructive pulmonary disease. *Eur Respir J* 2004; 24: 137–142.